

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the Application:

1-198. (Canceled)

199. (Currently amended) A pharmaceutical composition comprising:

~~_____ (i) a substrate in the form of bilayer vesicle membrane surface comprising:~~

~~at least one first surface building amphipathic substance selected from lipids and lipoids, capable of forming membrane bilayers a phosphatidylcholine; and~~

~~at least one second surface destabilizing amphipathic substance selected from surface active substances, a nonionic detergent, wherein the nonionic detergent destabilizes the vesicle, and~~

~~_____ wherein a macromolecule is bound to the surface of the vesicle; and~~

~~_____ (ii) an aqueous [a] liquid medium, wherein the second substance is more soluble than the first substance in the liquid medium, and~~

~~(ii) at least one third amphipathic substance selected from insulin, interferon, interleukin, immunoglobulin and hormone;~~

~~_____ the molecules of the third substance associated with the substrate;~~

~~wherein the substrate and the at least one third substance do not have opposite charges; and~~

~~wherein the composition is obtainable by steps comprising~~

~~_____ selecting the at least one first and the at least one second substance;~~

~~_____ combining the first and second substances in contact with the liquid medium to form substrates;~~

~~_____ selecting the at least one third substance;~~

~~_____ addition of the at least on third substance to the substrates preformed by the at least one first and the at least one second substance; and~~

~~_____ allowing the molecules of the third substance to associate with the substrate.~~

200. (Canceled)

201. (Currently amended) The composition of claim 199 wherein the substrate surface of the vesicle ~~formed by the first and second substance carry~~ carries a net electric charge and wherein the ~~third substance~~ macromolecule carries a net electric charge, ~~the molecules of the third substance associating with the substrate,~~ and the net electric charge density of the substrate surface of the vesicle and the net electric charge of the ~~molecules associating with the substrate~~ having macromolecule have the same sign.

202. (Currently amended) The composition of claim 199 wherein the substrates surface of the vesicle ~~formed by the first and second substance are~~ is negatively charged and wherein the ~~third substance~~ macromolecule is negatively charged.

203. (Canceled)

204. (Canceled)

205. (Canceled)

206. (Currently amended) The composition of claim 199 wherein the surfactant nonionic detergent ~~is selected from the group, consisting of a long-chain fatty acid; acids or a long-chain fatty alcohol; alcohols, alkyltrimethyl ammonium salts, alkyl dimethyl ammonium salts, alkylmethyl ammonium salts, alkylsulphate salts, monovalent salts of cholate, deoxycholates, glycocholates, glycodeoxycholates, taurodeoxycholates, taurocholates, acyl dimethyl aminoxides, alkanoyl dimethyl aminoxides, dodecyl dimethyl aminoxide, an alkyl-N-methylglucamide; methylglucamides, an alkanoyl-N-methylglucamide; methylglucamides, N-alkyl N,N dimethylglycines, 3-(acyldimethylammonio) alkanesulphonates, N-acyl-sulphobetaines, a polyethylen-glycol-octylphenyl ether; ethers, nonaethyleneglycol-octylphenyl ether;[,] a polyethylene-acyl ether; ethers, a nonaethylen-dodecyl ether; ethers, a polyethyleneglycol-isoacyl ether; ethers, an octaethyleneglycol-isotridecyl ether;[,] a polyethylene-acyl ether; ethers, an octaethylenedodecyl ether;[,] a polyethyleneglycol-sorbitane-acyl ester; esters, polyethyleneglycol-polyethyleneglykol-20-monolaurate; (Tween~~

20), polyethyleneglycol-polyethyleneglycol-20-sorbitan-monooleate; ~~(Tween-80)~~; a polyhydroxyethylene-acyl ether; ~~ethers~~; a polyhydroxyethylene-lauryl ether; ~~ethers~~; a polyhydroxyethylenemyristoyl ether; ~~ethers~~; a polyhydroxyethylene-cetylstearyl ether; ~~ethers~~; a polyhydroxyethylene-oleoyl ether; ~~ethers~~; a polyhydroxyethylene-polyhydroxyethylen-4, or 6, or 8, or 10, or 12-lauryl ether; ~~ethers (Brij-series)~~; a Brij; Myrj 45; polyhydroxyethylen-8-stearate (Myrj-45); a polyhydroxyethylene-laurate; polyhydroxyethylen-laurates; a polyhydroxyethylene-oleate; polyhydroxyethylen-oleates; polyethoxylated castor oil 40; ~~(Cremophor-EL)~~; a sorbitan-monoalkylate; ~~sorbitane-monoalkylates~~; sorbitane-monolaurate;[,]
an acyl-N-methylglucamide; methylglucamides; an alkanoyl-N-methylglucamide; methylglucamides; decanoyl-N-methylglucamide;[,]
dodecanoyl-N-methylglucamide;[,]
alkyl-sulphates; alkyl-sulphate salts; lauryl-sulphate; oleoyl-sulphate; sodium-deoxycholate; sodium-glycodeoxycholate; sodium-oleate; sodium-taurate; fatty acid salts; sodium-elaidate; sodium-linoleate; sodium-laurate; lysophospholipids; n-octadecylene-glycerophosphatidic acid; octadecylene-phosphorylglycerol; octadecylene-phosphorylserine; n-acyl-glycero-phosphatidic acids; lauryl-glycero-phosphatidic acids; oleoyl-glycero-phosphatidic acid; n-acyl-phosphorylglycerol; lauryl-phosphorylglycerol; oleoyl-phosphorylglycerol; n-acyl-phosphorylserine; lauryl-phosphorylserine; oleo-yl-phosphorylserine; n-tetradecyl-glycero-phosphatidic acid; n-tetradecyl-phosphorylglycerol; n-tetradecyl-phosphorylserine; corresponding palmitoleoyl-, elaidoyl-, vaccenyl-lysophospholipids; and or a surface-active polypeptide polypeptides.

207. (Currently amended) The composition of claim 199 wherein the nonionic detergent is at least one first substance is a phosphatidylcholine and/or a phosphatidylglycerol and the at least one second substance is a lysophospholipid, a lysophosphatidic acid, methylphosphatidic acid, lysophosphatidylglycerol, lysophosphatidylcholine, a partially N-methylated lysophosphatidylethanolamine, a monovalent salt of cholate, deoxycholate, glycocholate, glycodeoxycholate, or a sufficiently polar sterol derivative, a laurate, myristate, palmitate, oleate, palmitoleate, elaidate or other fatty acid salt and/or a polyethyleneglycol-sorbitan-acyl ester Tween-, a Myrj-, or a Brij-type surfactant, a polyhydroxyethylene-8-stearate, a polyhydroxyethylene lauryl ether, or a polyethylene-glycol-octylphenyl ether, a nonaethylen-

glycol-octylphenyl ether, Triton, a fatty acid sulphonate, sulphobetaine, or an -N-glucamide or a sorbitan-sorbitane-monoalkylate nonionic detergent surfactant.

208. (Currently amended) The composition of claim 199 wherein the ~~third substance~~ macromolecule is a hormone.

209. (Currently amended) The composition of claim 199 wherein the ~~third substance~~ macromolecule is ~~insulin selected from~~ human recombinant insulin or humanized insulin.

210. (Currently amended) The composition of claim 199 wherein the ~~third substance~~ macromolecule is interleukin suitable for the use in humans or animals and is selected from the group comprising IL-2, IL-4, IL-8, IL-10, ~~and or~~ IL-12.

211. (Currently amended) The composition of claim 199 wherein the ~~third substance~~ macromolecule is ~~interferon selected from~~ interferon alpha, beta or and gamma.

212. (Currently amended) The composition of claim 199 wherein the ~~third substance~~ macromolecule is immunoglobulin (Ig) ~~selected from~~ IgA, IgG, IgE, IgD or IgM+IgM.

213. (Currently amended) The composition of claim ~~208~~199 wherein the ~~hormone~~ macromolecule is calcitonin.

214. (Canceled)

215. (Canceled)

216. (Canceled)

217. (Canceled)

218. (Canceled)

219. (Canceled)

220. (Canceled)

221. (Canceled)

222. (Canceled)

223. (Canceled)

224. (Canceled)

225. (New) A liposomal composition obtained by the method comprising:

(i) combining a phosphatidylcholine, a nonionic detergent, and an aqueous liquid medium under conditions sufficient to make a bilayer vesicle, wherein the nonionic detergent destabilizes the vesicle; and

(ii) allowing a macromolecule to bind to the surface of the vesicle.

226. (New) The composition of claim 199, wherein the phosphatidylcholine is from soybean.

227. (New) The composition of claim 199, wherein the nonionic detergent is a polyethyleneglycol-sorbitan-acyl ester.

228. (New) The composition of claim 227, wherein the polyethyleneglycol-sorbitan-acyl ester is polyethyleneglycol-20-sorbitan-monooleate or polyethyleneglycol-20-sorbitan-monolaurate.

229. (New) The composition of claim 199 wherein the nonionic detergent is a Brij-type.

230. (New) The composition of claim 199, wherein the nonionic detergent is a Myrj-type.

231. (New) The composition of claim 230, wherein the Myrj-type nonionic detergent is Myrj-45.

232. (New) The composition of claim 199, wherein the macromolecule is a protein.

233. (New) The composition of claim 199, wherein the macromolecule is a polynucleotide.

234. (New) The composition of claim 199, wherein the macromolecule is a polysaccharide.

235. (New) The composition of claim 232, wherein the protein is an enzyme, an interferon, an interleukin, an immunoglobulin, or a hormone.

236. (New) The composition of claim 232, wherein the protein is insulin.

237. (New) The composition of claim 225, wherein the macromolecule is a protein.

238. (New) The composition of claim 225, wherein the macromolecule is a polynucleotide.

239. (New) The composition of claim 225, wherein the macromolecule is a polysaccharide.

240. (New) The composition of claim 237 wherein the protein is an enzyme, an interferon, an interleukin, an immunoglobulin, or a hormone.

241. (New) The composition of claim 237, wherein the protein is insulin.

242. (New) A pharmaceutical composition comprising:

(i) a bilayer vesicle comprising:

a phosphatidylcholine; and

sodium cholate, wherein the sodium cholate destabilizes the vesicle, and

wherein a macromolecule is bound to the surface of the vesicle; and

(ii) an aqueous liquid medium.

243. (New) The composition of claim 242 wherein the surface of the vesicle carries a net electric charge and wherein the macromolecule carries a net electric charge, and the net electric charge of the surface of the vesicle and the net electric charge of the macromolecule have the same sign.

244. (New) The composition of claim 242 wherein the surface of the vesicle is negatively charged and wherein the macromolecule is negatively charged.

245. (New) The composition of claim 242 wherein the macromolecule is a hormone.

246. (New) The composition of claim 245 wherein the hormone is human recombinant insulin or humanized insulin.

247. (New) The composition of claim 242 wherein the macromolecule is interleukin suitable for the use in humans or animals and is IL-2, IL-4, IL-8, IL-10, or IL-12.

248. (New) The composition of claim 242 wherein the macromolecule is interferon alpha, beta or gamma.

249. (New) The composition of claim 242 wherein the macromolecule is immunoglobulin (Ig) IgA, IgG, IgE, IgD or IgM.

250. (New) The composition of claim 242 wherein the macromolecule is calcitonin.

251. (New) The composition of claim 242, wherein the phosphatidylcholine is from soybean.

252. (New) The composition of claim 242, wherein the macromolecule is a protein.

253. (New) The composition of claim 252, wherein the protein is an enzyme, an interferon, an interleukin, an immunoglobulin, or a hormone.

254. (New) The composition of claim 253, wherein the hormone is insulin.

255. (New) The composition of claim 242, wherein the macromolecule is a polynucleotide.

256. (New) The composition of claim 242, wherein the macromolecule is a polysaccharide.

257. (New) A liposomal composition obtained by the method comprising:

(i) combining a phosphatidylcholine, sodium cholate, and an aqueous liquid medium under conditions sufficient to make a bilayer vesicle, wherein the sodium cholate destabilizes the vesicle; and

(ii) allowing a macromolecule to bind to the surface of the vesicle.

258. (New) The composition of claim 257, wherein the macromolecule is a protein.

259. (New) The composition of claim 257, wherein the macromolecule is a polynucleotide.

260. (New) The composition of claim 257, wherein the macromolecule is a polysaccharide.

261. (New) The composition of claim 258 wherein the protein is an enzyme, an interferon, an interleukin, an immunoglobulin, or a hormone.

262. (New) The composition of claim 261, wherein the hormone is insulin.

263. (New) The composition of claim 225 wherein the nonionic detergent is a long-chain fatty acid; a long-chain fatty alcohol; an alkyl-N- methylglucamide; an alkanoyl-N--methylglucamide; a polyethylen-glycol-octylphenyl ether; nonaethylenglycol-octylphenyl ether; a polyethylene-acyl ether; a nonaethylen-dodecyl ether; a polyethyleneglycol-isoacyl ether; an octaethyleneglycol-isotridecyl ether; a polyethylene-acyl ether; an octaethylenedodecyl ether; a polyethyleneglycol-sorbitane-acyl ester; polyethyleneglycol-20-monolaurate; polyethyleneglycol-20-sorbitan-monooleate; a polyhydroxyethylene-acyl ether; a polyhydroxyethylene-lauryl ether; a polyhydroxyethylenemyristoyl ether; a polyhydroxyethylene-cetylstearyl ether; a polyhydroxyethylene-oleoyl ether; a polyhydroxyethylene-4, or 6, or 8, or 10, or 12-lauryl ether; a Brij-type nonionic detergent; a Myrj-type nonionic detergent; a Triton nonionic detergent; a polyhydroxyethylene-8-stearate; a polyhydroxyethylene-laurate; polyhydroxyethylene-oleate; polyethoxylated castor oil 40; a sorbitan-monoalkylate; sorbitane-monolaurate; an acyl-N-methylglucamide; an alkanoyl-N-methylglucamide; decanoyl-N-methylglucamide; dodecanoyl-N-methylglucamide; or a surface-active polypeptide.

264. (New) The composition of claim 225 wherein the nonionic detergent is a polyethyleneglycol-sorbitan-acyl ester, a Myrj- or a Brij-type nonionic detergent, a polyhydroxyethylene-8-stearate, a polyhydroxyethylene lauryl ether, a polyethylene-glycol-octylphenyl ether, a nonaethylenglycol-octylphenyl ether, a Triton nonionic detergent, or an -N-glucamide or a sorbitan-monoalkylate nonionic detergent.

265. (New) The composition of claim 225, wherein the nonionic detergent is a polyethyleneglycol-sorbitan-acyl ester.

266. (New) The composition of claim 265, wherein the polyethyleneglycol-sorbitan-acyl ester is polyethyleneglycol-20-sorbitan-monooleate or polyethyleneglycol-20-sorbitan-monolaurate.

267. (New) The composition of claim 225 wherein the nonionic detergent is a Brij-type.

268. (New) The composition of claim 225, wherein the nonionic detergent is a Myrj-type.

269. (New) The composition of claim 225, wherein the Myrj-type nonionic detergent is Myrj-45.

270. (New) The composition of claim 225, wherein the phosphatidylcholine is from soybean.

271. (New) The composition of claim 225 wherein the surface of the vesicle carries a net electric charge and wherein the macromolecule carries a net electric charge, and the net electric charge of the surface of the vesicle and the net electric charge of the macromolecule have the same sign.

272. (New) The composition of claim 225 wherein the surface of the vesicle is negatively charged and wherein the macromolecule is negatively charged.

273. (New) The composition of claim 225 wherein the macromolecule is a hormone.

274. (New) The composition of claim 273 wherein the hormone is human recombinant insulin or humanized insulin.

275. (New) The composition of claim 225 wherein the macromolecule is interleukin suitable for the use in humans or animals and is IL-2, IL-4, IL-8, IL-10, or IL-12.

276. (New) The composition of claim 225 wherein the macromolecule is interferon alpha, beta or gamma.

277. (New) The composition of claim 225 wherein the macromolecule is immunoglobulin (Ig) IgA, IgG, IgE, IgD or IgM.

278. (New) The composition of claim 225 wherein the macromolecule is calcitonin.

279. (New) The composition of claim 257, wherein the phosphatidylcholine is from soybean.

280. (New) The composition of claim 257 wherein the surface of the vesicle carries a net electric charge and wherein the macromolecule carries a net electric charge, and the net electric charge of the surface of the vesicle and the net electric charge of the macromolecule have the same sign.

281. (New) The composition of claim 257 wherein the surface of the vesicle is negatively charged and wherein the macromolecule is negatively charged.

282. (New) The composition of claim 257 wherein the macromolecule is a hormone.

283. (New) The composition of claim 282 wherein the hormone is human recombinant insulin or humanized insulin.

284. (New) The composition of claim 257 wherein the macromolecule is interleukin suitable for the use in humans or animals and is IL-2, IL-4, IL-8, IL-10, or IL-12.

285. (New) The composition of claim 257 wherein the macromolecule is interferon alpha, beta or gamma.

286. (New) The composition of claim 257 wherein the macromolecule is immunoglobulin (Ig) IgA, IgG, IgE, IgD or IgM.

287. (New) The composition of claim 257 wherein the macromolecule is calcitonin.